WORLD INTELLECTUAL PROPERTY ORGANIZATION International Bureau



INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(51) International Patent Classification 6:

A1

(11) International Publication Number:

WO 99/27987

A61M 15/00, 16/00, B05D 7/14, B65D

83/04, 83/06, 85/42

(43) International Publication Date:

10 June 1999 (10.06.99)

(21) International Application Number:

PCT/US98/24914

(22) International Filing Date:

24 November 1998 (24.11.98)

(30) Priority Data:

08/982,320 09/184,821 2 December 1997 (02.12.97)

US 2 November 1998 (02.11.98) US

(81) Designated States: AU, BR, CA, CN, CZ, FI, HU, ID, IL, IS, JP, KP, KR, MX, NO, NZ, PL, RO, RU, SG, SK, TR, UA, VN, European patent (AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE).

Published

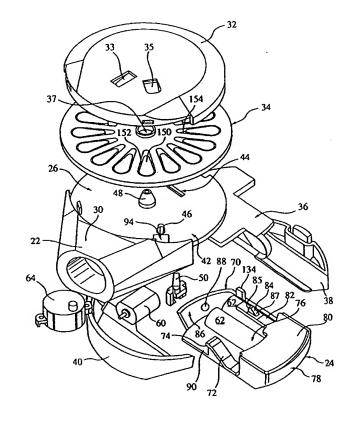
With international search report.

- (71) Applicant: DURA PHARMACEUTICALS, INC. [US/US]; 7475 Lusk Boulevard, San Diego, CA 92121-4204 (US).
- (72) Inventors: JACKSON, Thomas, R.; P.O. Box 2956, San Diego, CA 92038 (US). DAVIES, Karen; 7475 Lusk Boulevard, San Diego, CA 92121 (US). CHEN, Jeff; 2370 Watson Court, Palo Alto, CA 94303 (US). LIGOTKE, Mike; 7475 Lusk Boulevard, San Diego, CA 92121 (US). CAMERON, Allan; Suite A, 880 Hampshire Road, Westlake Village, CA 91361 (US).
- (74) Agents: OHRINER, Kenneth, H. et al.; Lyon & Lyon LLP, Suite 4700, 633 West Fifth Street, Los Angeles, CA 90071-2066 (US).

(54) Title: DRY POWDER INHALER

(57) Abstract

A dry powder inhaler (20) with a slider (24) for incrementally advancing a blister disk (34), for providing doses of dry powder medicament, with the blister disk (34) rotatably supported by a spindle (48) on a deck plate (42) of the inhaler (20). The deck plate (42) has a powder port (94), an advance slot (44). and a lifter slot (46) extending through the deck plate (42). The slider (24) attached to the deck plate (42) is movable between an open, and closed position. When the slider (24) opens, the lifter (50) moves up the ramp (72) of the slider (24) shearing open a blister (39), the blister (39) contents mix with air, and are then inhaled by a patient. As the slider (24) moves back to the closed position, the lifter (50) withdraws, and an advancing finger (84) turns the blister disk (34) to the next blister (39), positioning the blister (39) for opening, to provide the next dose to the patient. A turbine (230) spins up to a high speed driven by the flow of the patient's inhalation. The turbine (230) is connected to a shaft (246) to turn a propeller (226) located within a mixing chamber (224).



FOR THE PURPOSES OF INFORMATION ONLY

Codes used to identify States party to the PCT on the front pages of pamphlets publishing international applications under the PCT.

\L	Albania	ES	Spain	LS	Lesotho	SI	Slovenia
AM	Armenia	FI	Finland	LT	Lithuania	SK	Slovakia
AT	Austria	FR	France	LU	Luxembourg	SN	Senegal
AU	Australia	GA	Gabon	LV	Latvia	SZ	Swaziland
AZ	Azerbaijan	GB	United Kingdom	MC	Monaco	TD	Chad
BA	Bosnia and Herzegovina	GE	Georgia	MD	Republic of Moldova	TG	Togo
BB	Barbados	GH	Ghana	MG	Madagascar	TJ	Tajikistan
BE	Belgium	GN	Guinea	MK	The former Yugoslav	TM	Turkmenistan
BF	Burkina Faso	GR	Greece		Republic of Macedonia	TR	Turkey
BG	Bulgaria	HU	Hungary	ML	Mali	TT	Trinidad and Tobago
BJ	Benin	IE	Ireland	MN	Mongolia	UA	Ukraine
BR	Brazil	IL	Israel	MR	Mauritania	UG	Uganda
BY	Belarus	IS	Iceland	MW	Malawi	US	United States of America
CA	Canada	ΙT	Italy	MX	Mexico	UZ	Uzbekistan
CF	Central African Republic	JP	Japan	NE	Niger	VN	Viet Nam
CG	Congo	KE	Kenya	NL	Netherlands	YU	Yugoslavia
СН	Switzerland	KG	Kyrgyzstan	NO	Norway	zw	Zimbabwe
CI	Côte d'Ivoire	ΚP	Democratic People's	NZ	New Zealand		
CM	Cameroon		Republic of Korea	PL	Poland		
CN	China	KR	Republic of Korea	PT	Portugal		
CU	Cuba	KZ	Kazakstan	RO	Romania		
C7.	Czech Republic	LC	Saint Lucia	RU	Russian Federation		
DE	Germany	LI	Liechtenstein	SD	Sudan		
DK	Denmark	LK	Sri Lanka	SE	Sweden		
EE	Estonia	LR	Liberia	SG	Singapore		

1

DESCRIPTION

DRY POWDER INHALER

Background Of The Invention

5

10

15

20

25

30

The field of the invention is inhalers for delivering dry powder drugs to the lungs. Inhalers have long been used to deliver drugs into a patient's lungs. Typically, an inhaler provides a mixture of drugs and air or propellant gases. The mixture is delivered via the patient inhaling from a mouthpiece on the inhaler, for treatment of various conditions, for example, bronchial asthma. However, delivery of drugs via inhalation can be used for many other treatments, including those unrelated to lung condition.

Metered Dose Inhalers (MDIs) have been widely used for many years. MDI's typically dispense a single dose of a drug together with a propellant gas, with each actuation of the device. However, the propellant gases have been linked to destruction of the earth's ozone layer. In addition, with MDI's, the drug is generally released upon actuation of the device, regardless of whether the patient is properly inhaling during release. The patient may therefore not receive a complete dose unless the patient coordinates inhalation with actuation of the device. Achieving this coordination may be difficult for young children, or for patients with disabilities or under duress. Dry powder inhalers, on the other hand, do not have these disadvantages. Still, with dry powder inhalers, technical challenges remain in providing a reliable and simple to use device which can consistently deliver correct dosages of drugs.

One well known dry powder inhaler, the Diskhaler, described in U.S. Patent No. 4,627,432, uses individual drug doses sealed within blisters on a blister disk. A plunger pierces the blisters, to release each dose. The disk is advanced by a knob with each successive dose. The Spiros inhaler, described in U.S. Patent No. 5,622,166 (incorporated herein by reference) is a dry powder inhaler which also uses a blister disk. Blisters are opened via shear tabs on the blister disk. The disk is advanced to provide the next dose by sliding the mouthpiece cover between open and closed positions. While these types of devices may have met with varying degrees of success, disadvantages remain in indexing or advancing a blister disk within an inhaler, with opening the blisters to access the drug contents, with reliably providing intended dosages, and in other areas.

Accordingly, it is an object of the invention to provide an improved dry powder inhaler.

Statement Of The Invention

To these ends, a drug dose carrier, such as a blister disk, is advantageously rotatably supported on or in a dry powder inhaler for pharmaceuticals. A slider is preferably attached to a housing or deck plate of the inhaler, and is movable between opened and closed positions. The slider may advantageously contain batteries or other electronic components electrically linked to components positioned in the main body of the inhaler via a flex circuit. Movement of the slider between the open and closed positions, in a preferred embodiment, opens a container on the carrier disk to release a pharmaceutical powder for inhalation. Preferably, this movement also advances the carrier, in preparation for delivery of a subsequent dose.

In a second aspect of the invention, a propeller spins within a mixing chamber and is turned by a turbine driven by the patient's inhalation.

15

20

25

10

5

Brief Description Of The Drawings

Fig. 1 is a perspective view of the inhaler of the invention with the slider in the closed or first position;

Fig. 2 is a perspective view thereof with the slider in the open or second position;

Figs. 3A and 3B are exploded top and bottom perspective views of the inhaler shown in Figs. 1 and 2;

Figs. 4A and 4B show enlarged perspective views of components of the inhaler of Figs. 3A and 3B;

Fig. 4C is a perspective view of the lifter shown in Fig. 4A;

Fig. 5 is a top perspective view of the deck plate shown in Figs. 3A and 3B;

Fig. 6 is a bottom perspective view thereof;

Fig. 7 is a section view thereof taken along a lateral centerline;

Fig. 8 is a perspective view of the flex circuit shown in Figs. 3A and 3B;

Figs. 9 and 10 are perspective views of the disk and cover shown in Figs. 3A, 3B and 4A;

30

20

- Fig. 11 is a cross section view thereof taken through the anti-back up pawl shown in Fig. 9;
 - Fig. 12 is a central cross section thereof;
 - Fig. 13 is an exploded perspective view of a blister disk;
- 5 Fig. 14 is a top view thereof;
 - Fig. 15 is a section view thereof;
 - Fig. 16 is an exploded perspective view of another embodiment having a turbine in place of an electric motor;
 - Fig. 17 is a perspective view of the inhaler shown in FIG. 16;
- Fig. 18 is a perspective view thereof, also showing internal turbine details;
 - Fig. 19 is a schematic view showing air flow through the inhaler; and
 - Fig. 20 is an enlarged view of details shown in Fig. 19.

Detailed Description Of The Drawings

Turning now in detail to the drawings, the inhaler 20 includes a mouthpiece 22, and a slider 24, movable between a closed position, as shown in Fig. 1, and an open position as shown in Fig. 2. A handle 77 may be provided on the slider 24.

Turning to Figs. 3A, 3B and 5-7, a deck plate 42 has a flat top surface 26 and a flat bottom surface 28. A spindle 48 extends upwardly from the top surface 26 of the deck plate 42. A lifter slot 46 passes through the deck plate 42. An advancing slot 44 extends through the deck plate parallel to the direction of motion of the slider 24. A blister disk 34 used with the inhaler 20 includes a plurality of drug containing blisters 39 mounted on tabs 50, as described, for example, in U.S. Patent No. 5,622,166, incorporated herein by reference.

Turning momentarily to Figs. 13, 14 and 15, the blister disk 34 is made of a metal foil ring 200 having generally conical blisters 37 radially and equally spaced apart. The metal foil ring 200 and a seal ring 202 are adhered or bonded onto a carrier disk 204. The disk 204 is preferably plastic. The carrier disk 204 has tabs 150 pivotably attached to the disk 204 via flex joints 152. A blister 39 is aligned over each tab 150. The flex joints 152 hold the tabs 150 into a flat, in-plane position, but allow the tabs 150 to pivot about the

10

15

20

25

30

flex joints 152, with nominal torque. As shown in Fig. 15, powdered drug 205 is contained within each blister 39.

A cover 32 is attached over the top surface of a blister disk 34 to form a cover/disk assembly or unit 45. The blister disk 34 has a central opening 37 so that it can be mounted on and rotate around the axis of the spindle 48 which is normal to the axis of motion of the slider. The cover 32 itself latches onto the deck and does not rotate. The cover 32 retains the blister disk onto the deck as the blister disk rotates. Referring specifically to Figs. 3B and 5-7, a back rim 104 extends downwardly from the deck plate 42, opposite from the mouthpiece 22. A recess 102 in the deck plate 42 and back rim 104 allows for the motion of a latch 55 to lock the disk/cover assembly 45 onto the inhaler 20 when the cover blister disk assembly 45 is replaced by the user. A slider guide plate 114 extends downwardly from the bottom surface 28 of the deck plate 42. Slider lever guides 112 similarly are positioned on the bottom surface 28 of the deck plate 42, parallel to the advancing slot 44. Lifter guides 108 forming leg slots 110 are also attached to the bottom surface 28 of the deck plate 42 under the lifter slot 46, as best shown in Fig. 6. The leg slots 110 define the degree of freedom for the lifter motion.

A powder port 94 extends downwardly through the deck plate 42 and into an air passage 92 formed on the underside of the deck plate 42, heading to an aerosolizing or mixing chamber 106. The mouthpiece is advantageously removably attached to the deck plate 42. The spindle 48, back rim 104, slide guide plate 114, lever guides 112, and lifter guides 108 are preferably integral with the deck plate.

Referring back to Figs. 3A, 3B, 4A and 4B, the slider 24 includes a slider frame 70 attached to a bottom plate 90, forming a battery compartment 76. A lifter ramp 72 is attached or formed along one side of the slider bottom plate 90. A lifter 50, as shown in Figs. 4A, is slidably attached to the ramp 72. The lifter 50 includes L-legs 52 for holding the lifter 50 onto lips 74 on the ramp 72 and for retracting the lifter 50 from its raised position. The lifter 50 has a flat top surface 51 and an angled surface 54. The lifter ramp 72 passes under the lifter 50 as the slider 24 moves in and out. The lifter ramp 72 defines the cam profile which induces vertical motion in the lifter 50 as a result of the horizontal motion of the slider 24.

Referring to Figs. 3A, 4A and 4B, a slider cover plate 80 is attached to the slider frame 70, at the front or outside end 78 of the slider. A leg 82 on the slider cover plate 80

10

15

20

25

30

extends inwardly toward the rear end 86 of the slider 24. A spring biased or resilient advancing finger 84 having a flat back surface 85 and an angled front surface 87 projects upwardly from the leg 82. A battery check button extends through an opening 88 in the rear end 86 or bottom side 90 of the slider. As shown in Figs. 3A and 3B, a rear housing section 38 and a front housing section 40 are attached to the bottom surface of the deck plate 42, on either side of the slider 24, to enclose the inhaler and capture the slider in its guides, allowing only one degree of freedom. The front end 78 and rear end 86 of the slider are preferably shaped to match the contours of the inhaler.

A mechanical stop 134 on the slider engages a ledge 136 on the deck plate, to limit the outward sliding movement of the slider. Finger ridges or gripping features 75 may be provided on the bottom of the slider, as shown in Fig. 3B.

Referring to Figs. 3A, 3B and 8, a flex circuit 36 includes a battery plate 120 having battery slots 122. A circuitry area 126 is electrically connected to the battery plate 120 by a flexible ribbon 128. A switch 124 projects from the battery plate 120. An LED plate 130 and a motor lead tab 132 are provided as part of the circuitry area 126. A microprocessor 160 and memory chip 162 are provided on the circuitry area.

Turning to Figs. 9-12, a blister crushing rib 170 projects downwardly from the underside of the cover 32. The crushing rib 170 is positioned so that when the cover/blister disk assembly 45 is assembled onto the inhaler 20, the rib 170 aligns just behind the powder port 94. A tab return spring 35 extends downwardly inside the cover 32. The tab return spring 35 pushes downwardly on the inner end of the tab on the blister disk 34, which is aligned over the lifter 50 and lifter slot 46. An anti-backup pawl 33 also extends down inside the cover 32. The pawl 33 has a foot 175 with a flat front surface 177 and an angled or ramp rear surface 179.

Disk clips 176 having angled bottom facing surfaces are spaced apart around the inside of the cover 32, on a cylindrical rim wall 186. A front latch 180 and a rear latch 182 are provided for attaching the cover 32 to the inhaler 20. Various latch designs may be used. Turning momentarily to Fig. 3A, the front latch fits into or engages a raised area 30 between the mouthpiece 22 and the disk assembly 45.

Referring to Figs. 10 and 12, a central hub 188 extends down from the center inside surface of the cover 32. A blister disk 34 and a cover 32 are attached together to form an assembly 45 by aligning the central opening 37 or disk hub 190 of the disk with

6

the hub 188 on the cover, and then pressing the disk into the cover. As this occurs, the clips 176 spring slightly apart, due to the natural resiliency of the cover material, and then snap back into place, thereby holding the disk and cover together. Once they are snapped together, they are substantially permanently yet rotatably attached to each other. As shown in Fig. 12, the disk 34 may have a perimeter recess 208, such that the disk clips 176 clip onto a perimeter lip 210 around the outside of the disk.

5

10

15

20

25

30

As shown in Fig. 12, the disk hub 190 and cover hub 188 generally align but do not necessarily engage each other. The disk 34 floats somewhat in the cover. When installed, the disk centers itself on the spindle 48.

Referring once again to Figs. 3A and 3B, an electric motor 60 is connected to batteries 62 in the slider 24 via the battery plate 120, ribbon 128 and circuitry area 126 and motor lead tabs 132, which have electrical conductors within them. A breath actuated switch or sensor 64 also attached to the deck plate 42 and flex circuit senses pressure at the mouthpiece 22, and in response to sensed inhalation signals a microprocessor 160, which switches on the motor 60. The motor 60 spins an impeller within the mixing chamber 106, as described in U.S. Patent No. 5,577,497, incorporated herein by reference.

A label 100, shown in phantom line in Fig. 2, may be attached to the top of the cover 32, to identify its contents, and to close off the openings where the pawl 33 and return spring 35 attach to the cover.

In use, the blister disk 34 is provided as an assembly 45 with the cover 32 attached. The cover 32 captures the blister disk 34 and secures them together. Hence, the cover 32 and blister disk 34 are handled as a unit or assembly by the patient. The cover protects the top and sides of the blister disk 34 from damage during handling. The patient attaches the cover/disk assembly 45 to the inhaler 20 via a bayonet, latch, rocker, or other attachment feature, such as the latches 180, 182. The cover 32 allows the blister disk 34 to rotate on the spindle 48 while the cover itself is irrotatably snapped onto the deck plate. The cover is oriented so that the tab return spring 35 is located over the lifter slot.

With the cover/blister disk unit 45 secured to the inhaler 20 on top of the deck plate 42, the inhaler 20 is ready for use. The patient pulls the slider 24 from the first or closed position shown in Fig. 1 to the second or open position shown in Fig. 2. Sliding movement of the slider is guided by the lever guides 112 and slider guide 114 and the covers 40 and 38. Finger grips 76 or a handle 77 may be provided on the slider 24 to

10

15

20

25

30

better facilitate pulling the slider out. The slider 24 moves out until the mechanical stop 134 on the slider frame 70 contacts the stop or ledge 136 on the deck plate 42.

As the slider 24 is withdrawn, the lifter 50, which is held in position by the lifter guides 108, rides up on the lifter ramp 72. This ramp lifting movement causes the angled top surface 54 of the lifter 50 to rise up and protrude through the lifter slot 46 in the deck plate 42. The flat top surface 51 of the lifter 50 pushes against the underside of a tab 150 on the blister disk 34, causing a blister positioned over the tab to shear open, as the tab pivots about flex joints 152 which attach the tab to the disk 34. As the tab pivots, the angled surface 54 of the lifter engages the tab and continues to pivot it about the joints 132. As the blister shears open, the powdered pharmaceutical 205 contained within the blister falls into the powder port 94 and air passage 92, as described in U.S. Patent No. 5,622,166.

As the slider 24 is pulled out to the open position, the advancing finger 84 also moves down under the deck plate 42, as it recedes out of the advance slot 44.

The lifter 50 is restrained against lateral or longitudinal movement, by the engagement of the L-legs around the lips 74 on the lifter ramp 72 and by the lifter guides 108. Accordingly, the lifter 50 can move only vertically up or down.

The patient then inhales on the mouthpiece 22. The inhalation is sensed by the pressure switch 64 which turns on the motor 60. The motor spins the impeller within the mixing chamber 106 creating an aerosol of air and powdered drug, as described in U.S. Patent No. 5,577,497. The inhalation draws substantially all of the drug from the powder port 94 and staging chamber 92 into the mixing chamber 106, for inhalation. When inhalation is complete, the pressure switch 64 shuts off the motor 60. Inhalation preferably occurs when the slider is in the "out" position, when the blister is open and the inhaled air flow can draw any remaining drug out of the blister.

The patient next moves the slider 24 from the open position shown in Fig. 2 back to the closed position shown in Fig. 1. This movement is achieved by pushing on the slider front end 78. As the slider moves back into the closed position, the lifter 50 is pulled down on the ramp 72. The top surface 51 of the lifter 50 retracts to a position flush or below flush with the top surface of the deck plate 42. The cam profile of the lifter ramp 72 is designed to allow the lifter 50 to return to its neutral (down) position before the blister disk is incrementally advanced. The tab return spring 35 exerts a downward force

WO 99/27987

5

10

15

20

25

30

on the tab, to push the tab back into a horizontal orientation. The tab return spring also helps to keep the disk flat against the deck, by exerting a downward spring force on the disk. The cover hub 188 also exerts a downward force on the disk as well.

At the same time, the advancing finger 84 moves into the advance slot 44 and flexes or springs upwardly. The flat back surface 85 of the advancing finger protrudes upwardly through the advance slot 44 and extends into a tab slot 154 on the blister disk 34. Continued closing movement of the slider 24 drives the advancing finger to rotate the disk 34. The blister crushing rib 170 crushes down the conical point of the blister. This provides a visual indication through the transparent cover that the dose in that blister has been used and allows the patient to easily visually check the number of remaining doses on the disk. With the slider 24 completely moved back to the closed position, the advancing finger 84 turns the disk 34 through an angle which brings the next subsequent blister tab 150 into alignment with the lifer slot 46 and powder port 94.

As the disk advances by one position, the foot 175 of the anti-backup pawl 174 rides up and out of the slot 154 and then drops back down into the next slot. The flat front surface 177 of the foot prevents reverse (clockwise when view from above) movement, while the ramp 179 on the back surface allows the foot and pawl to temporarily deflect up to allow the disk to advance in the forward direction.

The flex circuit 36 provides electrical connections between the batteries 62, motor 60, switch 64, and other components, such as lamp indicators, microprocessor, memory chips, etc. The ribbon 128 on the flex circuit 36 allows the batteries and slider to remain electrically connected to the other fixed components, as the slider 24 is moved between open and closed positions. This motion can also be accomplished with flexible wires or cables.

The microprocessor controls the motor via the breath sensor; counts doses delivered; signals low battery voltage; checks battery voltage, and controls LEDS which indicate use conditions of the inhaler.

The in and out movement of the slider is simple and easily achieved by almost all patients. It also provides for a reliable and compact design. Inadvertent actuation is also largely eliminated.

Turning now to Fig. 16, a turbine driven inhaler 210 has a mouthpiece 214 attached to a body 212. A mouth piece cover 216 is attached to the mouth piece 214 via a

10

15

20

25

30

hinge 215. The mouth piece cover 216 can be pivoted open or removed during inhalation, or for cleaning.

A blister disk 218 having a transparent cover 220 is mounted over a disk plate 222 attached to the body 212. An aerosolizing chamber 224 is formed in the front wall of the body 212. These features may be similar to those shown in Fig. 4C.

A turbine 230 supported on the underside of the disk plate 222 has a turbine shaft 246 extending forwardly into the aerosolizing chamber 224. A propeller 226 is mounted on the forward end of the turbine shaft 246 in the aerosolizing chamber 224. A lower housing 232 encloses the bottom section of the disk plate 222. A plunger 234 extends through the lower housing 232, for opening blisters on the blister disk 218. The body 212 and lower housing 232 form an inhaler housing 211.

The design details and operation of the inhaler 210 are similar to the inhalers described in U.S. Patent Nos. 5,622,166. However, the inhaler 210 has no motor, batteries, switch or circuitry. Rather, the spinning propeller 226 is powered purely by the turbine 230.

Referring to Fig. 17-20, the turbine 230 has a cylindrical turbine housing 240. A stator 52 is joined to the turbine housing 240 near the turbine inlet 242. A turbine outlet 244 is preferably positioned on one side of the cylindrical turbine housing 240, at the outlet end 45 of the turbine 230. The turbine shaft 246 is rotatably supported within the turbine housing 240 via a bushing 248 near the outlet end 245, and via a needle bearing 250 near the inlet end 242. A rotor 254 having pitched turbine blades 256 is attached and centered on the turbine shaft 246 adjacent to the stator 252.

Turning to Figs. 19 and 20, and air inlet path 236 extends from the outside environment into the inhaler 210, and to the inlet end 244 of the turbine 230. A turbine outlet duct or path 260 runs from the turbine outlet 44 to a dump chamber 262 in the body 212 of the inhaler 210. An aerosolizing chamber duct 264 extends from the dump chamber 262 to the aerosolizing chamber 224. A chamber wall 215 in the mouth piece 214, as shown in Fig. 16 forms the front wall of the aerosolizing chamber 224, when the mouth piece 214 is attached on to the body 212. Openings in the chamber wall 215 allow the drug/air mixture to flow from the aerosolizing chamber 224 through the mouth piece 214 to the patient.

10

15

20

25

30

In use, a dose of dry powered drug is delivered into the dump chamber 262 from the blister disk 218, as described in U.S. Patent Nos. 5,622,166. The patient places the lips over the mouth piece 214 and inhales. Upon inhalation, ambient air flows through the inlet air path 236 to the inlet end 242 of the turbine 230. The air flowing at right angles to the plane of the rotor 254 rapidly spins up the rotor and turbine shaft 246, simultaneously rapidly spinning up the propeller 226 which is directly mounted on to the front end of the turbine shaft 246. The rotor blades are pitched so that the air flow through the turbine, parallel to the axis of the turbine shaft, exerts torque, causing the rotor to spin. Air flows out of the turbine outlet 244 to the dump chamber 242. Dry powder pharmaceutical particles are entrained in the air flow and carried through the aerosolizing chamber duct 264 into the aerosolizing chamber 224. The particles are de-agglomerated and mixed with air in the aerosolizing chamber 224. The air and particles pass out of the aerosolizing chamber 224 through openings in the chamber walls 215 and into the patient's mouth, throat, and lungs.

Preferably, the turbine is designed to that the turbine shaft will spin at from 5,000-15,000 rpm with an inspiration flow rate of 20-40 liters per minute. Most preferably, the turbine 30 is designed so that it spins up to 10,000 rpm or greater, within 100 milliseconds, with an inspiration flow rate of about 30 liters per minute. The stator 252 may have fixed vanes to better direct air flow to the rotor 254. Additional rotors 254 may optionally be added to the shaft 246.

The air flow through the inhaler 210 is substantially sealed, so that all air inhaled by the patient passes through the inlet air path 236, the turbine 230, the turbine outlet duct 260, the aerosolizing chamber duct 264, the aerosolizing chamber 224, and out through the mouth piece 214. For embodiments not having a separate dump chamber, air flowing out of the turbine may go directly into the aerosolizing chamber. Alternatively, a fraction of the total airflow into the patients lungs may be either inletted or channeled through ducts in the mouthpiece or inhaler to help beneficially entrain, mix, or guide the particle laden air mixture.

The turbine 230 may advantageously be provided as a separate subassembly installed into the inhaler 210 during manufacture. As a result, various other components of the inhaler, not requiring the precision tolerances necessary in the turbine, can be

manufactured and assembled separately. The turbine is compact, preferably having a housing diameter of 1-2 centimeters.

As shown in FIGs. 19 and 20, the dry powder does not flow through the turbine 230. Rather, the turbine 230 is upstream from the powder. The turbine therefore avoids clogging, friction, or bearing failure from powder particles, as the turbine is upstream of the powder. Although the turbine 230 uses the same air flow which entrains the powder, no balancing of air flow paths is required, and no coordination or timing of the spin-up of the turbine is needed, as the turbine automatically spins up upon inhalation.

5

10

15

20

25

30

The inhaler 210 consequently provides advantages of a motorized inhaler, without the need for a motor or batteries. If electronics are desired to provide an interface with the patient (for example, for dose counting, etc.) then very small batteries may be included to provide the typical low power requirements for such circuitry.

It may be desirable to allow the turbine enough time to reach a minimum acceptable rotary speed to de-agglomerate the drug, before the drug has passed through and out of the aerosolization chamber. One technique for this is to delay the introduction of the pharmaceutical mixture into the aerosolization chamber by sizing the length and diameter of the air path leading to the dump chamber. This allows the turbine time to reach the desired minimum rotational speed. As one example, if the outlet duct 260 is 1cm diameter and 2.5 cm long, during the initial period of inhalation, at a flow rate of 5 liters per minute, the air takes 24 ms to reach the aerosolizing chamber. During that interval the turbine has accelerated up to a sufficient minimum speed.

Alternatively the inhaler may be inverted so that the air flowing through the turbine and hence 'over' the open well containing the blister has to reach a high enough velocity (i.e., 223 liters per minute, depending on how the local geometry is configured) to lift the particles out of the blister well due to Bernoulli's principal, rather than the particles just falling out of the well due to gravity even before the inhalation has begun. This could act as a passive method for regulating when the drug is introduced to the system based on the airflow rate.

In another embodiment intended to have the drug particles exposed to the spinning propeller in the aerosolization chamber is to place the restrictor holes, or outlet holes, near the center of the chamber rather than at the periphery. This would act like a centrifugal size filter, i.e. the larger particles would be forced to the periphery where the most

aggressive de-agglomeration takes place until they are small enough to reach the more centralized outlet holes.

The turbine 230 may replace the motor in the inhalers shown in Figs.1-7 or in the above referenced U.S. Patents.

Claims

5

- 1. An inhaler for pharmaceuticals, comprising:
- a housing;
- a slider slidably attached to the housing;
- a ramp and an advancing finger attached to the slider; and
- a lifter slidably attached to the housing and to the ramp.
- 2. The inhaler of claim 1 further comprising a battery compartment in the slider.
- 3. The inhaler of claim 2 further comprising a flex circuit connecting the battery compartment in the slider to the housing.
- 4. The inhaler of claim 3 wherein the flex circuit includes a battery plate in the battery compartment of the slider, a ribbon joined to the battery plate, and a circuitry area in the housing joined to the ribbon, and with electrical conductors extending through the battery plate, ribbon, and circuitry area, thereby providing continuous electrical contact between the circuitry area and the battery plate with the slider in the first and second positions.
 - 5. The inhaler of claim 1 further comprising a mouthpiece attached to the housing.
- 6. The inhaler of claim 1 wherein the slider is slidable from a first position
 substantially within the housing to a second position extending substantially outside of the housing, with movement from the first position to the second position driving the lifter to engage the carrier disk, and wherein movement of the slider from the second position to

the first position causes the advancing finger to advance through the advancing slot in the deck plate, driving the disk to rotate the disk through an angular motion to a next position.

- 7. The inhaler of claim 1 further comprising a carrier disk rotatably supported on the housing, the carrier disk having a plurality of equally spaced apart openings and with a tab carrying a blister pivotally attached to the carrier disk within the openings.
- 8. The inhaler of claim 1 further comprising a deck plate in the housing, the deck plate including an advance slot and a lifter slot, with the advancing finger passing through the advance slot when the slider is in the first position, and with the lifter passing through the lifter slot, when the slider is in the second position.
- 9. The inhaler of claim 7 wherein the deck plate has a top surface and a bottom surface, a spindle extending upwardly from the top surface for mounting a carrier disk, and a slider guide extending downwardly from the bottom surface, for guiding the slider.
- 10. The inhaler of claim 8 further comprising an lifter guide on the bottom surface of the deck plate, the lifter guide restraining the lifter in position, except along its path of motion.
 - 11. The inhaler of claim 8 further comprising a mixing chamber in the housing, a motor in the housing and an impeller on the motor, with the motor electrically connected to the flex circuit.
- 20 12. The inhaler of claim 8 further comprising a first mechanical stop and a second mechanical stop on the housing for limiting travel of the slider into and out of the housing.

- 13. An inhaler for pharmaceuticals, comprising:
- a deck plate having a first side and a second side;
- a spindle on the first side of the deck plate;
- a powder port, an advancing slot, and a lifter slot, adjacent to the powder port, each extending through the deck plate;
 - a blister disk rotatably supported on the spindle, with the blister disk having a plurality of equally spaced apart openings;
 - a slider attached to the deck plate and movable between a first position and a second position;
- a ramp on the slider;

20

- a lifter slidably mounted on a frame on the second side of the deck plate and on the ramp on the slider, the frame allowing the lifter to move only along a specific path of motion towards and away from the lifter opening; and
- an advancing arm on the slider biased upwardly against the second side of the deck plate and aligned with the advancing opening.
 - 14. The inhaler of claim 12 wherein the advancing arm converts linear motion of the slider to rotational motion of the blister disk.
 - 15. A cover/disk unit for storing a dry powder pharmaceutcal, comprising: a blister disk having a metal foil ring and a seal ring bonded on a carrier disk;
- a plurality of generally conical blisters formed on a first side of the blister disk, with each blister containing a dose of a dry powder pharmaceutical sealed within the foil ring and the seal ring;
 - a cover on the blister disk and covering the first side of the blister dis; and means for holding the cover onto the disk while allowing the disk to rotate.
- 25 16. The cover/disk unit of claim 14 wherein the means for holding comprises at lest one clip on the cover.

- 17. The cover/disk unit of claim 14 wherein the means for holding comprises a hub on the cover extending into an opening in the disk.
- 18. The cover/disk unit of claim 14 further comprising a cylindrical rim wall on the cover extending over the side edges of the disk.
- 5 19. A cover/blister disk unit for use with a dry powder inhaler, comprising: a disk having a plurality of blisters holding a dry powder pharmaceutical; and a rigid cover privotably and permanently attached to one side of the disk over the blisters.
- The inhaler of claim 1 further comprising a carrier disk rotabtably supported on the housing, the carrier disk having a plurality of equally spaced apart
 openings and with a tab carrying a blister pivotally attached to the carrier disk within the openings.
 - 21. The inhaler of claim 5 further comprising a cover attached to the carrier disk.
 - 22. An inhaler comprising:
- 15 a housing;
 - an aerosolizing chamber within the housing;
 - a propeller within the aerosolizing chamber;
 - a turbine adjacent to the aerosolizing chamber, the turbine having an inlet side and an outlet side;
- a turbine shaft extending out of the turbine and into the aerosolizing chamber, with the propeller mounted on the turbine shaft;
 - a first air pathway extending from an air inlet in the housing to an inlet side of the turbine; and

a second air pathway extending from the outlet side of the turbine to the aerosolizing chamber.

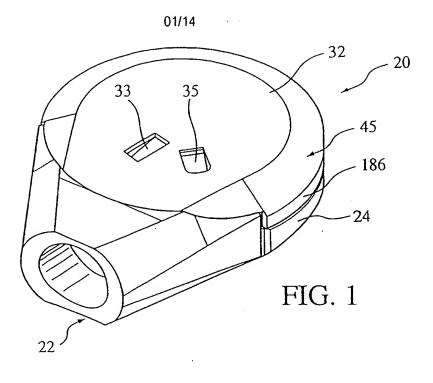
- 23. The inhaler of claim 22 further comprising a stator on the turbine and a rotor on the turbine shaft.
- 5 24. The inhaler of claim 22 wherein the turbine outlet is oriented at an angle to the turbine inlet.
 - 25. The inhaler of claim 22 wherein the turbine is configured to spin the turbine shaft at from 5000 to 15000 rpm with a flow rate of 20-40 liters/minute of air flowing through the turbine.
- 10 26. The inhaler of claim 22 further comprising a dump chamber in the second air pathway, between the turbine outlet and the aerosolizing chamber.
 - 27. A method of providing a dose of an inhaled pharmaceutical to a patient, comprising the steps of:

providing a pharmaceutical powder into an aerosolizing chamber in an inhaler; drawing air through a turbine as the patient inhales, thereby spinning a propeller, attached to the turbine, in the aerosolizing chamber;

mixing air and the pharmaceutical powder in the aerosolizing chamber via the spinning propeller.

28. The method of claim 27 wherein the air is drawn through the turbine in a direction perpendicular the plane of a rotor in the turbine.

- 29. The method of claim 27 further comprising the step of drawing air out of the turbine and through a dump chamber holding a dose of a pharmaceutical.
- 30. The method of claim 27 wherein the pharmaceutical powder is mixed with air flowing out of the turbine, to avoid having the powder contact the turbine.
- 5 31. The inhaler of claim 22 further comprising a rotor attached to the turbine shaft, with the turbine shaft and rotor having an axis of rotation parallel to the direction of air flow through the turbine.



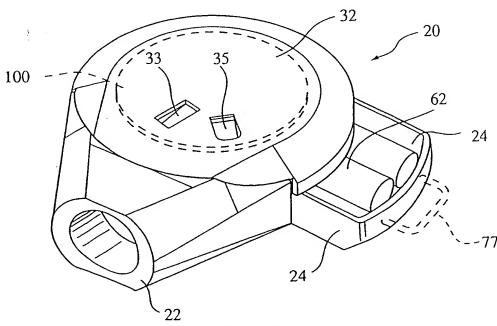


FIG. 2

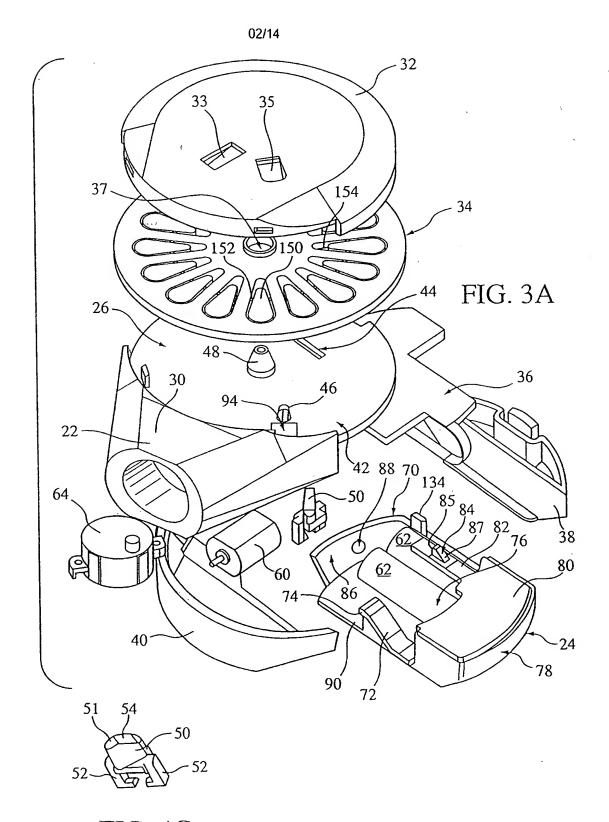


FIG. 4C

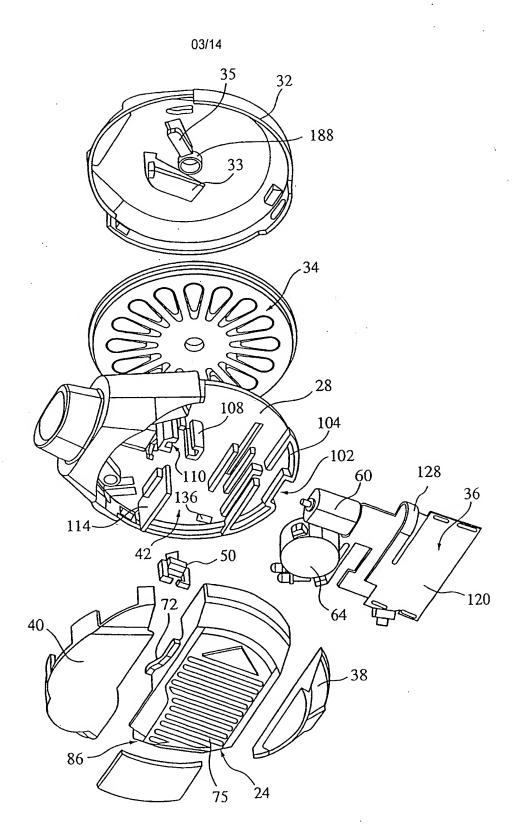
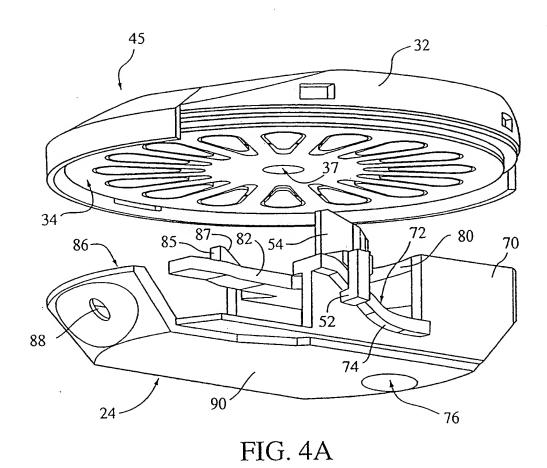


FIG. 3B SUBSTITUTE SHEET (RULE 26)



05/14

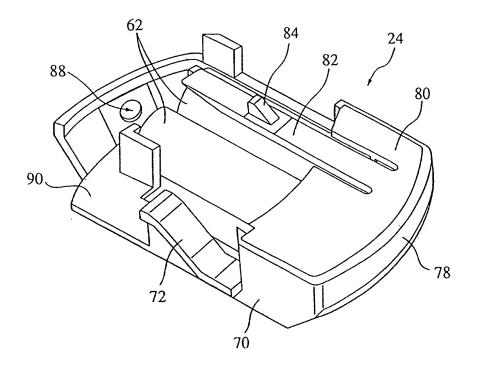


FIG. 4B

06/14

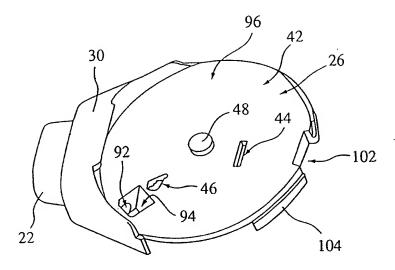


FIG. 5

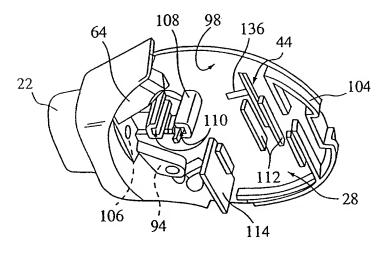
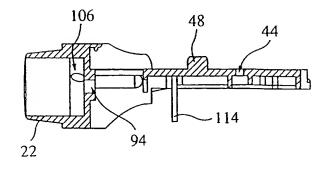


FIG. 6



 $FIG.\ 7 \\ \text{SUBSTITUTE SHEET (RULE 26)}$

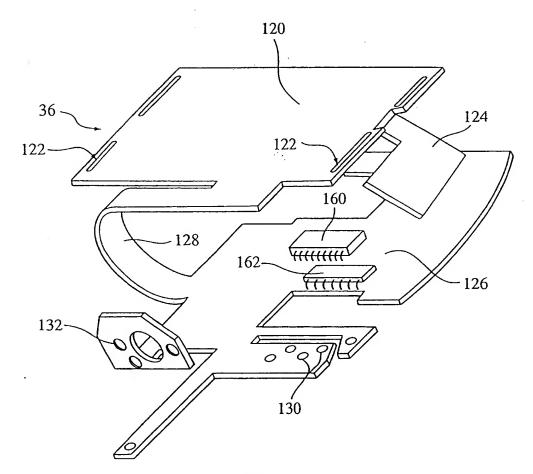


FIG. 8

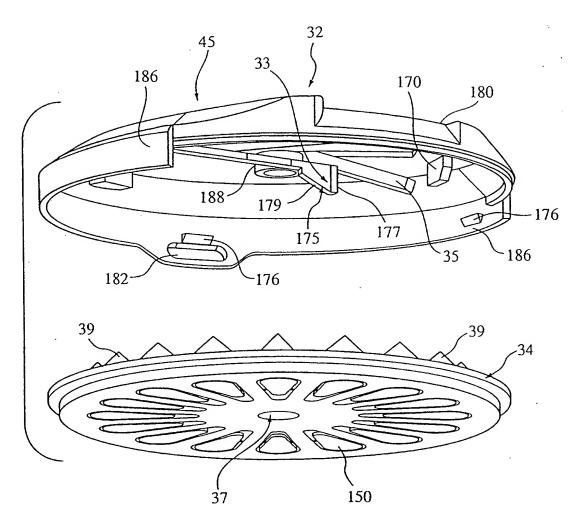


FIG. 9

09/14

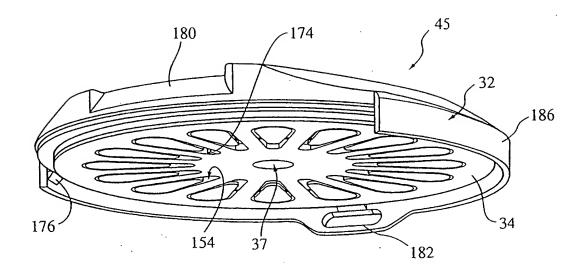
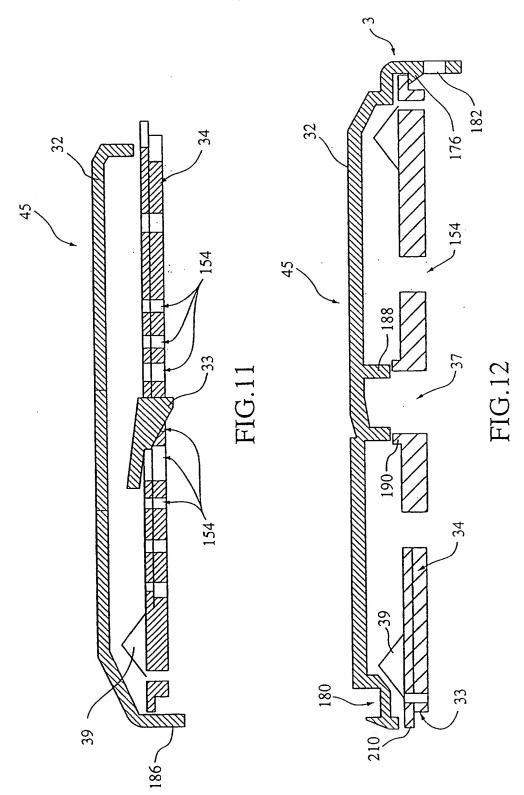


FIG. 10





SUBSTITUTE SHEET (RULE 26)

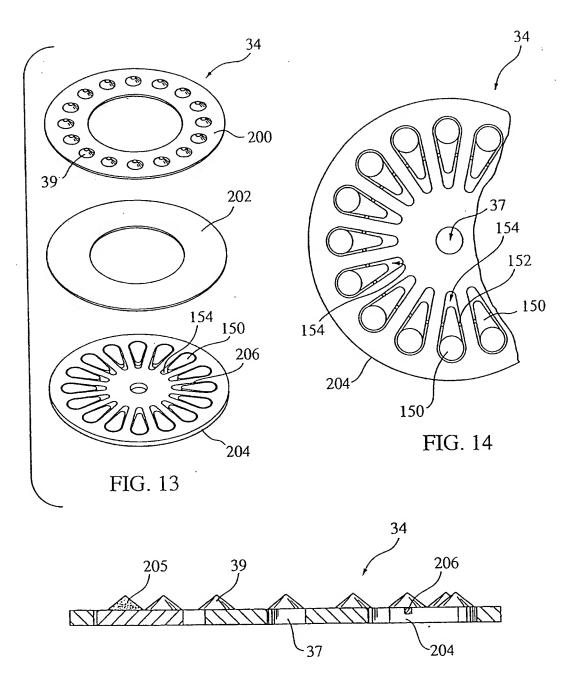


FIG. 15

SUBSTITUTE SHEET (RULE 26)

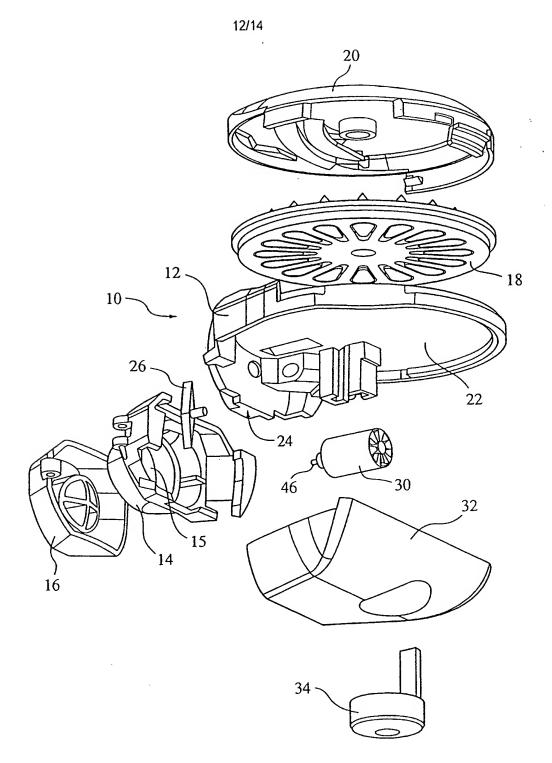
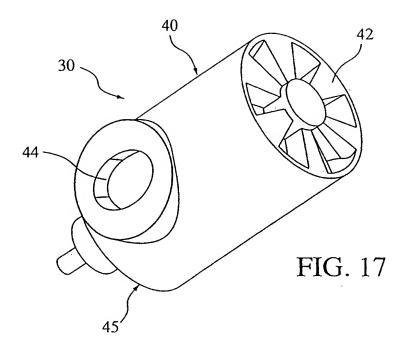
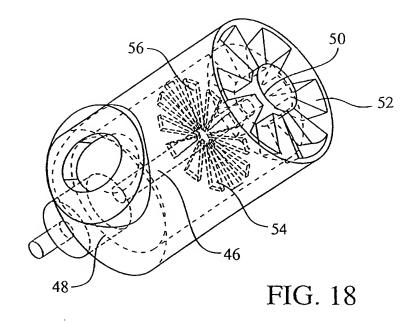


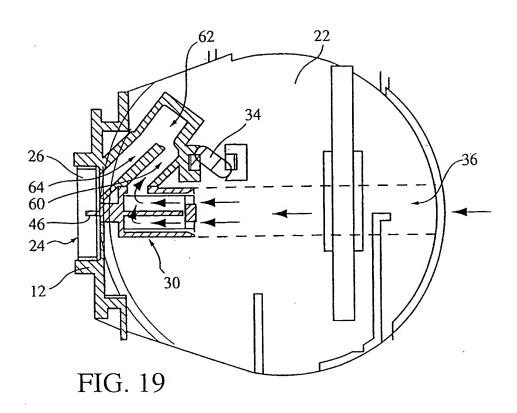
FIG. 16

SUBSTITUTE SHEET (RULE 26)





14/14



64 62 34 60 24 FIG. 20

SUBSTITUTE SHEET (RULE 26)

INTERNATIONAL SEARCH REPORT

International application No. PCT/US98/24914

A. CLASSIFICATION OF SUBJECT MATTER IPC(6) : A61M 15/00, 16/00; B05D 7/14; B65D 83/04, 06, 85/42									
US CL :128/203.15. 203.21; 206/531, 532 According to International Patent Classification (IPC) or to both national classification and IPC									
B. FIELDS SEARCHED									
Minimum documentation searched (classification system followed by classification symbols)									
U.S.: 128/200.14, 203.12, 203.15, 203.19, 203.21 203.23; 206/469, 531, 532, 538, 540									
Documentati	on searched other than minimum documentation to the o	extent that such documents are included in	the fields searched						
Electronic data base consulted during the international search (name of data base and, where practicable, search terms used) APS									
Search Terms: inhaler or inhalers, battery, housing, draw, ramp									
C. DOCUMENTS CONSIDERED TO BE RELEVANT									
Category*	Citation of document, with indication, where ap	propriate, of the relevant passages	Relevant to claim No.						
X	US 4,811,731 A (NEWELL et al.) 14	1, 5, 6, 20							
	and col. 3, lines 34-65.		2-4						
Y			2-4						
Y	US 5,327,883 A (WILLIAMS et al.) 1 65, and col. 8, lines 29-36	2-4							
X	US Des. 384,283 A (DAVIES et al.) 3 1-5.	14-19							
Purther documents are listed in the continuation of Box C. See patent family annex.									
Special categories of cited documents: T' later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention									
.E. ear	be of particular relevance	ne claimed invention cannot be seed to involve an inventive step							
cit sp	cument which may throw doubts on priority claim(s) or which is ad to establish the publication date of another citation or other acial reason (as specified)	"Y" document of particular relevance; the considered to involve an inventive	s step when the document is						
m	cument referring to an oral disclosure, use, exhibition or other cans cument published prior to the international filing date but later than	th documents, such combination the art							
th	priority date claimed	Date of mailing of the international se							
08 JANUARY 1999 08 JANUARY 1999									
Name and mailing address of the ISA/US Commissioner of Patents and Trademarks Box PCT Washington, D.C. 20231 Authorized officer JOSEPH P. WEISS, JR.									
1	1- (702) 205 2220	Telephone No. (703) 308-0323							